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WILLIAM ROBERT BOON

20 March 1911–28 October 1994

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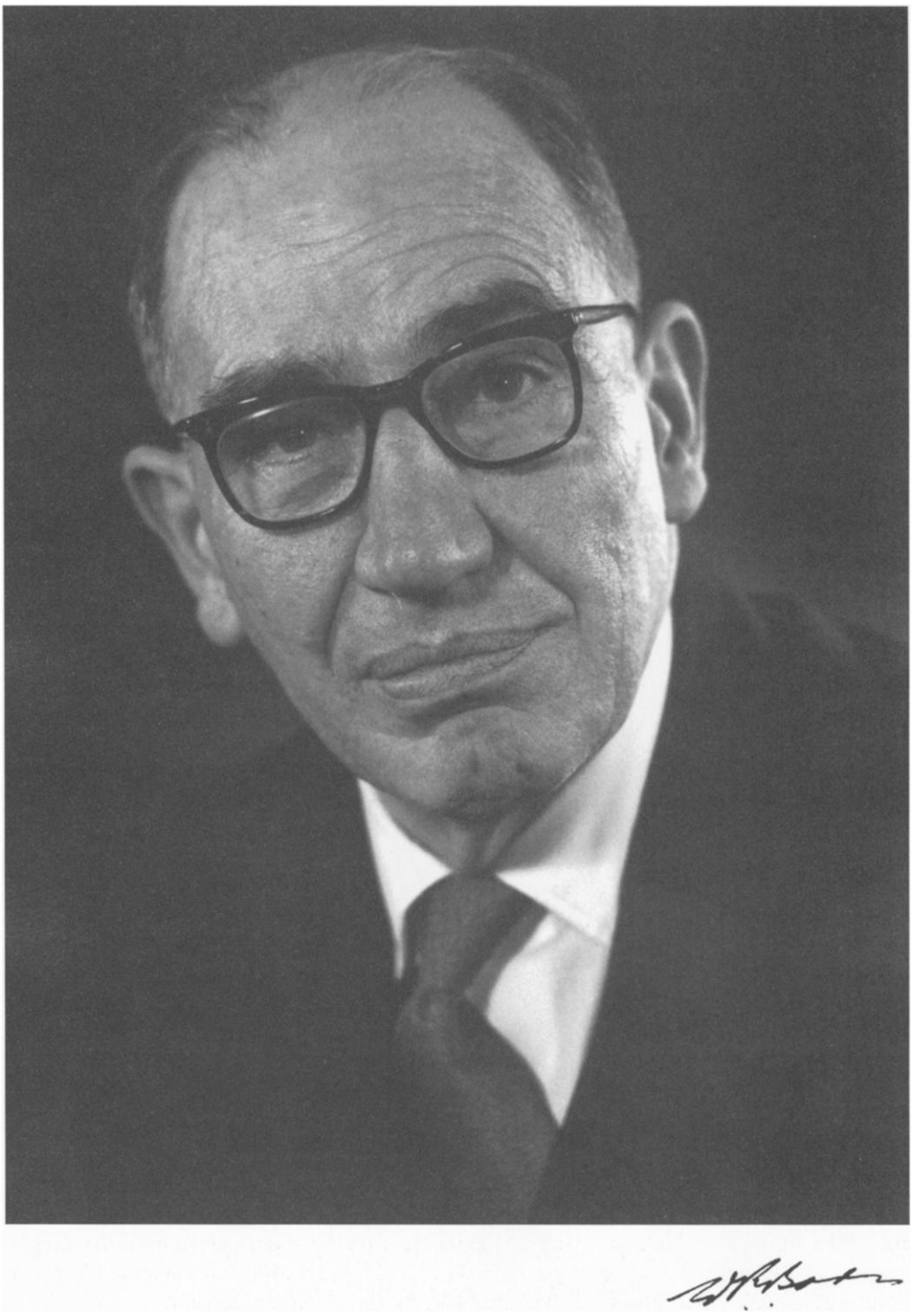
EARLY YEARS

William (Bill) Boon and his sister Jean were the children of Walter Boon, a general railway agent, and his wife Ellen Catherine, a farmer's daughter. Bill's mother and father were third cousins and their common great grandfather, James Medhurst, achieved local fame in Sussex as an amateur archaeologist. Some of the artefacts he discovered are in Worthing museum. James Medhurst was also a manufacturer of Tonbridge Ware, and pieces made by him are exhibited in the museum at Tunbridge Wells.

Boon received his early education in two private schools before entering St Dunstan's College, Catford. Professor H.E. Armstrong, F.R.S., was a governor of the school and encouraged science teaching based on the Heuristic method. Boon records that by the age of 14, he had developed a liking for chemistry, physics and mathematics.

In sports, he showed ability in cross country and middle distance running; he recalls that he was 'hopeless at cricket and slightly better at rugby football'. He became a member of the Officers' Training Corps at his school.

It was assumed that he would have a career with the railway business founded by his father, which involved collecting parcels in central London and redirecting them to the appropriate railway terminal. However, a reorganization of the railways in 1923 made such a career unlikely. Boon's chemistry master at St Dunstan's (W. Anderson) persuaded Bill's father to let him stay on at school and aim for a university education. Oxbridge was out of the question as he had no Latin, then obligatory, so he applied and was accepted by King's College, London, to read for an honours degree in chemistry. This he obtained in 1932, after which, in 1936, he obtained a Ph.D. in biochemistry, supervised by Dr (later Professor) W. Robson. At King's, his interest in cross country running and the O.T.C. continued and he became an Officer in Charge of an O.T.C. detachment in the funeral procession of King George V.



In 1938 he married a fellow King's College graduate, Marjorie Betty Oury, only daughter of Sydney and Florence Oury of Esher. Bill and Betty remained strong supporters of their College, and he regularly attended the annual Chemistry Dinner, in his later years leaning heavily on a walking stick.

Bill and Betty had three children, Sally, born in 1939, Michael Robert, 1942, and Heather Mary, 1948. Both daughters married Australians and Michael, since leaving Cambridge, has been employed by I.C.I.

Career at I.C.I.

On leaving university in 1936, Boon became one of a team of six Ph.D. chemists formed in the Dyestuffs Division at Blackley, Manchester, to explore the potential of pharmaceuticals. This Division was one of the four founding members of I.C.I. Boon's first assignment was to explore variations of Nikethamide, which, as a cardiac stimulant, produced an unfortunate convulsive effect when used at high dosages.

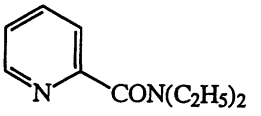


Figure 1. Structure of Nikethamide.

Although compounds less prone to this defect were discovered, the company decided to discontinue this project. With others, he then studied developmental processes for the manufacture of the antimalarial drug Mepacrine, and all stages of this synthesis were achieved on the plant scale.

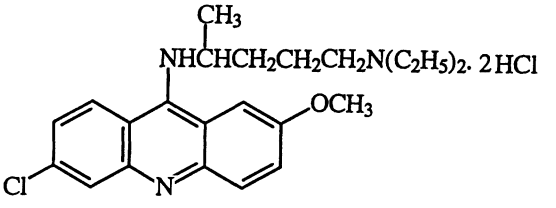


Figure 2. Structure of Mepacrine hydrochloride.

Penicillin investigations

In 1942, Boon was put in charge of a section to develop the production of penicillin, to purify it and attempt to determine its structure. At that time, the Forces' medical services were anxious to obtain this new antibiotic, not only for dealing with wound infections, but also for the treatment of syphilis and gonhorrhea, and the Ministry of Supply required it to be produced in quantity. It was believed that workers in the US were achieving improved production by submerged fermentation and Boon went there, with W.B. Hawes of Burroughs Welcome, to

obtain information on this development. They found that the major advances had been made at the Northern Regional Research Laboratory of the US Department of Agriculture at Peoria, using a different strain of *Penicillium notatum* and a cornsteep liquor with lactose instead of glucose in the medium. Visits were made to a number of other US manufacturers, two of which, Merck and Squibb, were using submerged fermentation on a pilot plant-scale.

On returning home, it was confirmed that submerged fermentation using the US strain of the fungus with cornsteep liquor and lactose gave improved results. Furthermore, mixing the Merck penicillin with the I.C.I. sample and submitting the mixture to chromatography produced a clean separation, thus confirming the existence of more than one penicillin.

However, due to urgent pressure from the Ministry of Supply, it was decided to set up a milk-bottle fermentation unit up to the maximum capacity available. This achieved an output of 300 mega units per week, and Boon states in his report that the penicillin produced in this Unit was probably the first to be used in the field in North Africa.

In the meantime, a Plant Design Committee was set up in the UK under Boon's chairmanship. He went again to the US, this time with H.J. Jephcott, Managing Director of Glaxo. They were impressed by Pfizer's achievements, and on their return Boon recommended that a new plant, based on submerged fermentation be constructed and that I.C.I. should seek a cooperation agreement with Pfizer.

About this time, the pure sodium salt of penicillin G was obtained by Levi, who also prepared the potassium and rubidium salts used by Dorothy Hodgkin in her crystallographic work.

H.C. Carrington joined the I.C.I. research group, and a contribution of some significance was made to determination of the structure of penicillin. It was known that penicillin was a mono basic acid and contained a 'hidden' carboxyl group, which was liberated on hydrolysis as carbon dioxide. At Boon's suggestion, penicillin methyl ester was made by reaction with diazomethane. Reaction of this ester with mercuric chloride liberated penicillamine methyl ester, thus proving the identity of the free carboxyl group. In the light of now-known structures, the above chemistry is indicated in figure 3.

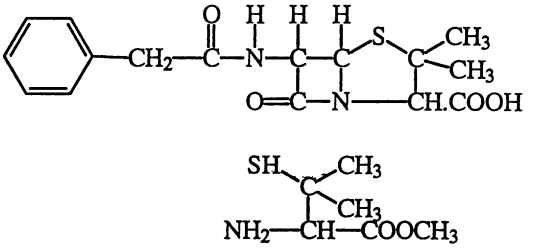


Figure 3. Structure of penicillin G (top) and methyl ester of penicillamine (bottom).

As penicillin became more widely used, there were many reports of excessive pain resulting from repeated injections, and this led to a widespread demand for pure penicillin. Chromatography was not feasible as a manufacturing procedure, but in the US some purification had been achieved by precipitating penicillin as its N-ethyl piperidine salt from amyl acetate solution. As piperidine was difficult to obtain in England, and to avoid patent complications, Boon suggested that the N-ethyl-hexamethylenetetramine salt should be considered. This alternative procedure proved just as effective, but unfortunately the 'pure' penicillin recovered from the salt was still unpleasant when injected into patients.

As research developed, the General Penicillin Committee decided that chromatographically pure penicillin should be pooled and recrystallized at the Peoria laboratory and that this should become the International Standard. The International Unit was subsequently defined as the activity contained in one 18,060th of a milligram of the International Standard.

Boon's next career move was to guide the research of a Section towards new synthetic drugs and chemicals for crop protection. Following the discovery of the anticonvulsive drug Mysoline, first made by H.C. Carrington, Boon initiated the synthesis of related compounds, some of which showed antimalarial or schistosomicidal activity. Unfortunately, these were found to be too toxic for clinical use.

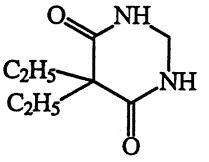
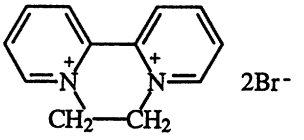


Figure 4. Structure of Mysoline.

A publication which described developments with the novel heterocyclic system pteridine, prompted Boon to ask G.R. Ramage to prepare and examine compounds based on hydroxy-pteridines. An unambiguous synthesis of 6-hydroxy pteridine arose from this work. When Ramage was appointed Professor of Chemistry at Salford, Boon continued this line of heterocyclic chemistry with others and a series of five papers were published.

THE DIPYRIDIL HERBICIDES

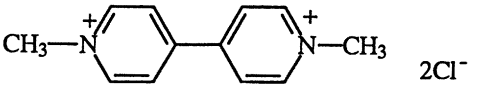
It was about this time that biological tests were made at I.C.I.'s Jealott's Hill Research Station on a number of quaternary ammonium compounds, some of which had shown herbicidal activity. It had also been observed that cationic surface active agents, such as cetyl trimethyl ammonium bromide, could cause foliage damage when used as wetting agents in sprays applied to plants. With these indications, R.L. Jones decided to obtain as many quaternary ammonium salts as were available in the specimen collection of I.C.I.'s Dyestuffs Division. When these were tested as herbicides by R.C. Brian at Jealott's Hill, he immediately recognized the outstanding herbicidal activity of one of them (Brian *et al.* 1958). This compound, now known as diquat, was the reaction product of 2,2'-dipyridyl and ethylene dibromide. It had been first synthesized by R.J. Fielding in a research laboratory of I.C.I.



1,1′-ethylene-2,2′ dipyridylium dibromide

Figure 5. Structure of diquat.

Further research on related compounds revealed a second important dipyridylium herbicide, which was given the name paraquat.



N,N´-dimethyl-4,4´-dipyridylium dichloride

FIGURE 6. Structure of paraquat.

Both these herbicides rapidly destroyed green plant tissue, but they lost their herbicidal activity when in contact with soil. Intensive studies were carried out by Boon's group on the mode of action of diquat and paraquat and on their uptake and movement in plants. It was established that the conditions most conducive to effective treatment are exposure to light and high atmospheric humidity, with the soil being dry and cold. It was also found that quaternary salts based on 2,2´- and 4,4´-dipyridyl could be converted by strong reducing agents into highly coloured radicals, and that only salts that could be reduced in this way were herbicidal. This formation of radicals is fundamental to the action of diquat and paraquat on plants, a mode of action which is activated by the photosynthetic and respiratory mechanisms of the plant.

In assessing all the research findings on diquat and paraquat, there were some serious doubts about their possible commercial value. Two other important herbicides, 2,4-D (2,4-dichlorophenoxyacetic acid) and MCPA (2-methyl-4-chlorophenoxy acetic acid), marketed by I.C.I., were selective, destroying a wide range of weed species in cereals without harming the crop plants. By contrast, diquat and paraquat were not selective, as both crop plants and weeds succumbed to treatment. Not only this, but, as already mentioned, studies on soil absorption showed these dipyridyls to have only a short life in soil. Although this property was good from the environmental viewpoint, it ruled out any possibility for diquat or paraquat being used as soil applied herbicides. In view of this and their lack of selectivity on plants, one can understand the I.C.I. Board showing little enthusiasm for their commercial development.

However, as Dr Brian relates, this assessment was strongly contested by Boon, who was excited by the fact that diquat and paraquat lost their herbicidal activity when in contact with soil. He was now a senior manager at Jealott's Hill and in a position to urge the company to exploit what he considered to be a lead towards a revolutionary system of agriculture. His vision was to use the herbicide on land after a cereal crop had been harvested; all the weed seedlings and other remaining vegetation would be destroyed and, within a few days, the herbicide in the soil would be inactivated leaving no harmful residue. A new crop could then be sown and the cost of ploughing and other cultivations would have been avoided. Furthermore, not disturbing the soil provided protection against soil erosion.

Fortunately for I.C.I. (now Zeneca) and for world agriculture, Boon's crusade was successful. Urgent steps were taken to step up the production of diquat and paraquat. Various problems had to be solved. The first diquat production was from 2,2´-dipyridyl bought in kilogram quantities from Switzerland. A later publication by G.M. Badger of Adelaide showed that 2,2´-dipyridyl could be made by heating pyridine under reflux with Raney nickel. With full particulars from Australia, this method was adopted and used at an I.C.I. plant set up at Huddersfield. However, Brian relates that during this episode Boon's enthusiasm

became an explosive reaction when he was told that the diquat pilot plant had caught fire, and was completely destroyed.

For making 4,4′-dipyridyl, a known reaction between pyridine and sodium could also lead to explosions. The difficulties were overcome, however, and the compound was made at a plant at Widnes yielding several hundred tons per year. Further research at I.C.I. by F.R. Bradbury and C.W. Suckling led to an improved process involving a reaction between pyridine and sodium in liquid ammonia and a plant with a capacity of 2000 tons output per year was erected. The product was quaternized with methyl chloride to yield paraquat. M.B. Green played an important part in this commercial development.

Other interests and achievements

Boon had become a leading scientific authority at I.C.I. and he received well-deserved recognition of his achievements. He was awarded the Mullard medal of the Royal Society, an Honorary D.Sc. degree from Cranfield and a British Crop Protection Medal. He was also a Visiting Professor at Reading University and a Fellow of King's College, London. His unrelenting and successful pressure for the dipyridyl herbicides to be developed commercially was well known, and to foster such determination in others he established a Boon Award for Perseverance at I.C.I. In retirement, he served as a member of both the Advisory Committee for the Research Councils and the Environmental Research Council.

Boon had various hobbies and interests. He was an accomplished linguist, photographer and cabinet maker. He made items of furniture for his and Betty's home and for those of their three children when they married. He also made an altar table for his local parish church. He shared with his wife an interest in music, opera and ballet.

Having met Bill Boon on only two occasions I have been most grateful in writing this memoir for information supplied by his wife, Betty, and Drs A. Calderbank, R.C. Brian, J.T. Braunholtz, J.M. Winchester, C.W. Suckling and M.B. Green, who were colleagues of his at I.C.I. All of them reveal a sincere respect and affection for a friend of strong personality and great vigour, admired as a charming and courteous person, who was well in the forefront of science and technology. And here, I record another aspect of Bill's personality, sent to me by his wife Betty:

> He had a tremendous sense of humour, which he never lost. He would joyfully tell the story of a little incident that occurred during a business visit to New York. In a rather grand hotel, where he was having coffee with a colleague, he was tempted to remove a piece from a suit of armour which was standing in the room and out of devilment slipped into it a sugar lump on which he had first put his signature. Next time he stayed at the same hotel, a year or more later, he lifted off the small piece of armour and took out the lump of sugar, saying gleefully to his companion 'It doesn't say much for their cleaner, does it!'

Sadly, he had a long battle with health problems following his retirement in 1973. He lost an eye as a result of glaucoma, and for the last six months at I.C.I. he was being treated for malignant hypertension. By 1977 he was in the final stage of renal failure and for the rest of his life was a dialysis patient. He died on 28 October 1994 leaving his son, two daughters and Betty, his wife of 56 years, who cared for him so devotedly during the period of his serious illness.

Acknowledgement

The frontispiece photograph was taken by the Godfrey Argent Studio, and given to the Royal Society in July 1974. It is reproduced with their permission.

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